

Serial No.: 08/648,270
Filed: May 15, 1996

~~37. A compound according to claim 36 wherein said base is selected from the group consisting of adenine, guanine, thymine, cytosine and uracil.~~

38. A compound according to claim 28 wherein said biological moiety is a phosphoramidite nucleoside.

C.1 cancelled
~~39. A compound according to claim 38 wherein the acetylene bond of said compound is attached to the base of said nucleoside.~~

40. A compound according to claim 30 wherein said base is selected from the group consisting of adenine, guanine, thymine, cytosine and uracil.

41. A compound according to claim 28 wherein said biological moiety is an amino acid.

42. A compound according to claim 28 wherein said biological moiety is a protein.

43. A compound according to claim 26 or 27 wherein M is selected from the group consisting of ruthenium, rhenium and osmium.--

REMARKS

Claims 26- 43 are in the case. The applicants thank the Examiner for pointing out the previous error in claim numbering.

The applicants thank the Examiner for his helpful comments in the telephone call on December 17, 1998, and for his inclusion of the Caruthers patent. As a result of that discussion, the pending claims have been cancelled, and new claims 26 to 43 have been added. The new claims are believed to overcome the rejections of record.

Support for the Z substituted aromatic group being a biological moiety is found on page 9, lines 15-29, page 10, lines 21-22, and page 13, lines 13-15, and throughout the

Serial No.: 08/648,270
Filed: May 15, 1996

specification.

Claim 5 is rejected under 35 U.S.C. §112, fourth paragraph, as being of improper dependent form. Claim 5 has been cancelled and thus the rejection should be withdrawn.

Claims 4-5, 91-10, 12-13 and 17-25 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for the recitation of "comprising" and "further comprising". The new claims do not recite these terms, and the Examiner's helpful comments in this regard are appreciated.

The Examiner reiterates the rejection of claims 4 and 5 on the basis that "it is unclear whether the instant claimed subject matter is properly included within the scope of the elected subject matter." The Examiner's position appears to be that the the original restriction was directed to phenanthroline compounds comprising nucleotides and nucleoside phosphoramidites, and thus the claims must be so restricted. However, as stated by the Examiner in the restriction dated May 20, 1997, linking claims are examined with the elected invention to the extent they apply. The genus claims need not be amended.

Claim 13 has been rejected for insufficient antecedent basis. This terminology has been amended in the new claims.

Claims 10 and 18 are rejected as reciting "the phosphoramidite form of the nucleotide". The new claims recite "phosphoramidite nucleosides", which as argued previously, comply with the art terminology (see Exhibit F of the previous response).

Claim 17 has been rejected as reciting "comprises the base of a nucleoside". This terminology has been amended in the new claims.

Claims 9, 10, 13, 17, 18, 19 and 21 are rejected under 35 U.S.C. §112, fourth paragraph, as being of improper dependent form. The applicants submit that the new claims obviate this rejection.

Claim 19 is rejected for reciting "nucleic acid" in a manner the Examiner feels is improper. This terminology has been amended in the new claims.

Serial No.: 08/648,270
Filed: May 15, 1996

New grounds of rejection under 35 U.S.C. §112, second paragraph

Claim 4 is rejected as not indicating where the "Z" substituent is attached to the triple bond. The applicants respectfully submit that this is clearly outlined in the specification; for example, on page 12, the attachment of uridine is shown, and on page 13, lines 7-12, the location of representative attachments to the other bases are outlined.

The duplication of claim 9 and 20 is noted and removed in the new claims.

The term "phosphoramidite form of the nucleoside" has been amended in line with the art accepted terminology of "phosphoramidite nucleoside"; see Exhibit F of the previous response.

The Examiner rejects claim 12 (new claim 26) on the basis that the "A-Y-B" terminology is unclear. While not agreeing with the propriety of the rejection, the claims have been amended to recite "A and B are each independently selected from carbon or nitrogen, Y is a bond, and the entire moiety may be selected from the group consisting of acetylene, alkene, azo or imine".

The use of "the" in claims 17-19 has been amended in the new claims.

The Examiner questions the limitation of the nucleosides in claims 22-25. The applicants point out that the claims are dependent, and as such, the scope of the independent claim can be construed broader, to include other nucleosides and nucleoside analogs.

Similarly, the applicants thank the Examiner for pointing out the incorrect use of base terminology in claims 22-25. The new claims recite the correct terms for the bases.

Claims 4-5, 9-10, 12-13 and 17-25 are rejected under 35 U.S.C. §112, first paragraph, as the disclosure is only enabling for non-nucleoside containing compounds. The Examiner states that the application does not disclose how to make phenanthroline linked nucleosides, etc.

However, the applicants respectfully submit that the specification outlines in great detail the methods used to make the compounds of the invention. For example, pages 17 to 21 of the specification describe the synthesis of the compounds. First, 1,10-

Serial No.: 08/648,270
Filed: May 15, 1996

phenanthroline is brominated at the 3 and/or 8 position using Scheme I outlined on page 17 (see line 5 to the end). Palladium-mediated cross coupling (a technique well known in the art as outlined on page 19, lines 6 - 18) is used to react the brominated 1,10-phenanthroline to a Z group comprising an aromatic acetylene; see page 18, lines 3-9 and Scheme II. Alternatively, the brominated 1,10-phenanthroline is reacted with an acetylene, which is then reacted with a halogenated aromatic Z group; see Scheme III.

The addition of metal ions and optional co-ligands is described on page 19, line 19 to page 20, line 1.

In general, as outlined on page 20, line 3-7, aromatic acetylenes are either commercially available or easily made using the described techniques.

The specific attachment of nucleosides, nucleotides and nucleic acids is discussed on page 20, line 8 to page 21, line 6. Halogenated nucleosides are commercially available, and thus are easily used without modification in Scheme III. Alternatively, brominated nucleosides can be reacted with acetylene to form an acetylene-nucleoside that then can be reacted using Scheme II. The phosphoramidate forms of these modified nucleosides are easily made, as the Examiner will appreciate.

Accordingly, the specification clearly enables making and using of the compounds containing nucleosides, nucleotides, nucleic acids, and phosphoramidate nucleosides.

As outlined in M.P.E.P. §2164.04, the applicants respectfully remind the Examiner that in order to make a rejection under 35 U.S.C. §112, first paragraph, the examiner has the initial burden of establishing a reasonable basis to question the enablement provided for the claimed invention.

Accordingly, as the specification provides the required enablement, the applicants submit that the rejection is improper and should be withdrawn.

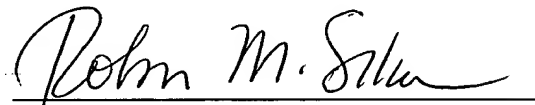
The applicants submit that the claims are now in condition for allowance and an early notification of such is solicited.

Serial No.: 08/648,270
Filed: May 15, 1996

If after review, the Examiner feels that there are unresolved issues, the applicants respectfully request a telephone interview with the undersigned.

Respectfully submitted,

FLEHR HOHBACH TEST
ALBRITTON HERBERT LLP



Robin M. Silva
Reg. No. 38,304

Four Embarcadero Center
Suite 3400
San Francisco, CA 94111-4187
Telephone: (415) 781-1989
Dated: 17 December 1998

573174